

### REMARKS

Claims 44, 45, 47, and 55-59 are pending in the application. Claims 44, 45, and 47 have been amended. Claims 42, 43, 46, and 48-54 have been cancelled without prejudice. New claims 55-59 have been added. Support for the amendments and new claims can be found in the specification at, e.g., page 4, lines 4-23, and page 23, lines 3-8. In addition, applicant submits a replacement sequence listing containing the sequences disclosed in the application as filed. No new matter has been added.

#### Objection to the Specification

At page 2 of the Office Action, the specification was objected to as failing to provide a sequence identifier for each individual sequence. A substitute sequence listing is enclosed with the present response. All sequences disclosed in the application and figures are contained in this substitute sequence listing. Furthermore, the sequence listing has been amended so that SEQ ID NO:1 corresponds to the sequence identified as SEQ ID NO:1 in Fig. 1. As a result of this amendment to the sequence listing, no correction of Fig. 1 is required.

Finally, Applicant submits amendments to the specification to correct the sequence identifiers throughout the specification. At page 5, SEQ ID NO:1 and SEQ ID NO:2 were switched to coincide with the sequences disclosed in Fig. 1. At pages 5, 8, 17 and 30-34, sequence identifiers were inserted following each sequence. No new matter has been added.

#### 35 U.S.C. §112, First Paragraph (Enablement)

At pages 2-5 of the Office Action, claims 42 and 45-47 were rejected as allegedly not enabled.

Claims 42 and 46 have been cancelled without prejudice, thereby obviating their rejection. Applicant respectfully traverses the rejection of the remaining claims in view of the claim amendments and the following remarks.

As amended, independent claims 44 and 45 are directed to methods of treating an immunological disorder by administering to a subject an effective amount of a composition comprising an antagonist antibody or antigen-binding fragment thereof that binds to KIM-1.

As detailed in the specification, the inventor of the present application has discovered that treatment of a mammal with a KIM-1 antagonist alters the interaction of T cells with other immune system cells and thereby strongly suppresses an IgG response to an antigen. Such treatment nearly eliminates IgG1 production by memory B cells in response to subsequent challenge with the antigen. In addition, blockade of the binding of KIM-1 to its receptor reduces secretion of IFN-gamma by immune cells engaged in an antigen response in the mixed lymphocyte response assay (antagonist anti-KIM-1 antibodies and KIM-1-Ig fusion protein exemplified in application) and is therapeutically effective in a mouse model of inflammatory bowel disease (KIM-1-Ig fusion protein exemplified in application). By virtue of the present application's demonstration that KIM-1 antagonists interfere with T cell activation, suppress IgG response to antigen, and are therapeutically effective in a mouse model of inflammatory bowel disease, the skilled person would have reasonably expected antagonist anti-KIM-1 antibodies to be effective in the treatment of inflammatory bowel diseases and the other immunological disorders recited in the claims. The experimental findings contained in the present application would have led the skilled person to conclude that KIM-1 antagonists would be broadly effective in the treatment of diseases in which a mammalian immune system attacks an inappropriate target, either through T cell cytotoxicity or through an immunoglobulin response.

The present rejection is based at least in part on the assertion (at page 3 of the Office Action) that "[t]he claimed anti-KIM-1 antibodies would encompass antibodies that act as agonists or antagonists." As noted above, the claims have been amended to require that the anti-KIM-1 antibodies (or antigen-binding fragments thereof) used in the claimed methods are "antagonists." In view of the biological assays described in the application, the skilled person would have had no difficulty in determining whether a given anti-KIM-1 antibody is an antagonist antibody. As a result, even if some anti-KIM-1 antibodies may have agonist activity, as is suggested by the Office Action's citation of several post-filing publications, it nonetheless

would have required only routine screening to select those antibodies that have antagonist activity and are useable in the claimed methods (and eliminate those antibodies having agonist activity). For example, a given anti-KIM-1 antibody could be tested in a mixed lymphocyte reaction as described in Example 11 to determine if the antibody reduces IFN-gamma secretion into the supernatant, as was the case for several anti-KIM-1 antibodies described in that working example. Example 11 clearly demonstrates that at least some anti-KIM-1 antibodies have antagonist activity. In addition, a given anti-KIM-1 antibody could be tested in a mouse model of inflammatory bowel disease (such as that described in Example 12) to determine if the antibody is therapeutically effective in the model system (as was the case for the KIM-1-Ig fusion protein exemplified in Example 12). In view of the specification's demonstration that antagonist anti-KIM-1 antibodies and a KIM-1-Ig fusion protein inhibited the production of proinflammatory mediators such as IFN-gamma, combined with the demonstration that the KIM-1-Ig fusion protein is therapeutically effective in a mouse model of inflammatory bowel disease, the skilled person would have reasonably expected that an antagonist anti-KIM-1 antibody would (like the KIM-1-Ig fusion protein) be effective in the treatment of inflammatory bowel diseases as well as the other immunological disorders recited in the claims.

In view of the claim amendments and the foregoing remarks, applicant respectfully submits that the person of ordinary skill in the art, at the time the present application was filed, would have been able to practice the claimed methods without undue experimentation and with a reasonable expectation of success. As a result, applicant requests that the Examiner withdraw the rejection.

35 U.S.C. §102(e) (Anticipation)

At page 5 of the Office Action, claims 42, 46, and 47 were rejected as allegedly anticipated by US20050014687.

Claims 42 and 46 have been cancelled without prejudice. Claim 47 has been amended to depend from independent claim 45, which claim was not rejected under this heading. It is applicant's understanding that these amendments obviate the present rejection.

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### CONCLUSIONS

Applicant respectfully submits that all grounds for rejection have been overcome and that all claims are now in condition for allowance.

Enclosed is a Petition for One Month Extension of Time. The extension of time fee is being paid concurrently herewith on the Electronic Filing System (EFS) by way of Deposit Account authorization. Please apply any other charges or credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 13751-055US1.

Respectfully submitted,

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/Jack Brennan/

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